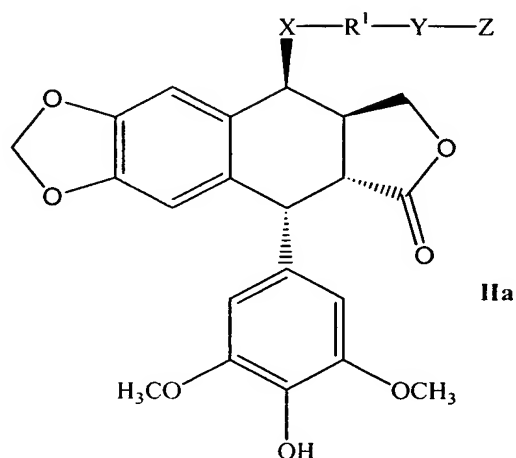


What is claimed is:

1. A compound selected from the group consisting of:

(i) compounds of **Formula IIa**:



5

wherein:

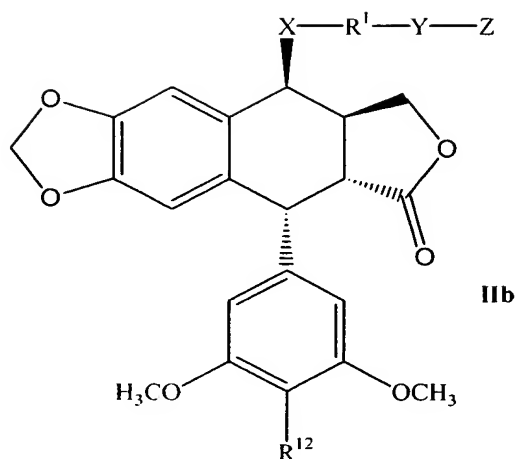
X is a linking group selected from the group consisting of -O-, -S-, -NH-, -CO-, -CH=N-, and CH₂NH-;

10 R¹ is a covalent linkage between X and Y, or is loweralkyl, loweralkenyl, or phenyl, and when phenyl is unsubstituted or is substituted from one to four times with loweralkyl, hydroxy, alkoxyl, alkylogen, alkylamino, alkyoxycarbonyl, amino, halogen, nitro, or nitrile;

Y is none, -NHCO-, -CONH-, -OCO-, or -COO-;

15 Z is -CHR²(CH₂)_nR³, where n is 0 to 8, or -(CH₂)_n- is incorporated into Z as a five-, six-, seven-, or eight-membered ring; R² is H, and R³ is a loweralkyl, loweralkenyl, aryl, lower alkylamino, lower alkenylamino, or arylamino; or a pharmaceutically acceptable salt thereof; and

(ii) compounds of **Formula IIb**:



wherein:

X is a linking group selected from the group consisting of -O-, -S-, -NH-, -CO-, -CH=N-, or CH₂NH-, and in one preferred embodiment is -NH-;

R¹ is a covalent linkage between X and Z, or is loweralkyl, loweralkenyl, or phenyl, and when phenyl is unsubstituted or is substituted from one to four times with loweralkyl, hydroxy, alkoxy, alkylogen, alkylamino, alkyoxycarbonyl, amino, halogen, nitro, or nitrile;

Y is none, -NHCO-, -CONH-, -OCO-, or -COO-;

Z is -(CH₂)_nR³, where n is 0 to 8, or -(CH₂)_n- is incorporated into Z as a five-, six-, seven-, or eight-membered ring. R³ is a loweralkyl, loweralkenyl, aryl, lower alkylamino, lower alkenylamino, or arylamino;

R¹² is -OR₄, -NR₄R₅, -OCOR₄, -OCOOR₄, -OCOSR₄, or -OCONR₄R₅, where R₄ and R₅ are selected from the group consisting of lower alkylamino, lower alkenylamino, and arylamino;

or a pharmaceutically acceptable salt thereof.

2. A compound according to claim 1, wherein X is -NH- and R¹ is phenyl.

3. A compound according to claim 1, wherein R¹ is phenyl.

4. A compound according to claim 1 having the structure of **Formula IIa**.

5. A compound according to claim 1 having the structure of **Formula IIb**.
6. A compound according to claim 1 selected from the group consisting of:
- 5 4'-*O*-Demethyl-4 β -[4''(tyramido)-anilino]-4-desoxy-podophyllotoxin (**5**);
- 4'-*O*-Demethyl-4 β -[4''-(phenylethylamido)-anilino]-4-desoxy-
podophyllotoxin (**6**);
- 4'-*O*-Demethyl-4'-(*N*', *N*'-dimethyl-glycyl)-4 β -(4''-nitroanilino)-4-desoxy-
podophyllotoxin (**8**);
- 10 4'-*O*-Demethyl-4'-(*N*', *N*'-dimethyl-glycyl)-4 β -(4''-fluoroanilino)-4-desoxy-
podophyllotoxin (**9**);
- 4'-*O*-Demethyl-4'-(*N*', *N*'-dimethyl-glycyl)-4 β -(4''-nitroanilino)-4-desoxy-
podophyllotoxin hydrochloride (**10**);
- 4'-*O*-Demethyl-4'-(*N*', *N*'-dimethyl-glycyl)-4 β -(4''-fluoroanilino)-4-desoxy-
15 podophyllotoxin hydrochloride (**11**);
- 4'-*O*-Demethyl-4'-glycyl-4 β -(4''-fluoroanilino)-4-desoxy-podophyllotoxin
(**13**);
- 4'-*O*-Demethyl-4'-sarcosyl-4 β -(4''-fluoroanilino)-4-desoxy-podophyllotoxin
(**14**);
- 20 4'-*O*-Demethyl-4 β -{[4''-(2'''-dimethylamino)-ethylamido]-anilino}-4-desoxy-
podophyllotoxin;
- 4'-*O*-Demethyl-4 β -{[4''-(4'''-methyl-piperazyl)-amido]-anilino}-4-desoxy-
podophyllotoxin;
- 4'-*O*-Demethyl-4 β -{[4''-(4'''-piperidinopiperidyl)-amido]-anilino}-4-desoxy-
25 podophyllotoxin;
- 4'-*O*-Demethyl-4 β -{[4''-N-(4'''-amino-1'''-benzylpiperidine)-amido]-anilino}-
4-desoxy-podophyllotoxin;
- 4'-*O*-Demethyl-4 β -{[4''-(4'''-nitrophenyl-piperazyl)-amido]-anilino}-4-
desoxy-podophyllotoxin;

4'-*O*-Demethyl-4 β -{[4''-N-(3'''-aminoquinuclidine)-amido]-anilino}-4-desoxy-podophyllotoxin;

4'-*O*-Demethyl-4'-[(2'''-dimethylamino)-ethoxyl]-4 β -(4''-fluoroanilino)-4-desoxy-podophyllotoxin; and

5 4'-*O*-Demethyl-4'-[(2'''-dimethylamino)-ethylamino]-4 β -(4''-fluoroanilino)-4-desoxy-podophyllotoxin.

7. A compound according to claim 1 selected from the group consisting of:

4'-*O*-Demethyl-4 β -[4''(tyramido)-anilino]-4-desoxy-podophyllotoxin (5);

10 4'-*O*-Demethyl-4 β -[4''-(phenylethylamido)-anilino]-4-desoxy-podophyllotoxin (6);

4'-*O*-Demethyl-4 β -{[4''-(2'''-dimethylamino)-ethylamido]-anilino}-4-desoxy-podophyllotoxin;

15 4'-*O*-Demethyl-4 β -{[4''-(4'''-methyl-piperazyl)-amido]-anilino}-4-desoxy-podophyllotoxin;

4'-*O*-Demethyl-4 β -{[4''-(4'''-piperidinopiperidyl)-amido]-anilino}-4-desoxy-podophyllotoxin;

4'-*O*-Demethyl-4 β -{[4''-N-(4'''-amino-1'''-benzylpiperidine)-amido]-anilino}-4-desoxy-podophyllotoxin;

20 4'-*O*-Demethyl-4 β -{[4''-(4'''-nitrophenyl-piperazyl)-amido]-anilino}-4-desoxy-podophyllotoxin; and

4'-*O*-Demethyl-4 β -{[4''-N-(3'''-aminoquinuclidine)-amido]-anilino}-4-desoxy-podophyllotoxin.

25 8. A compound according to claim 1 selected from the group consisting of:

4'-*O*-Demethyl-4'-(*N*', *N*'-dimethyl-glycyl)-4 β -(4''-nitroanilino)-4-desoxy-podophyllotoxin (8);

4'-*O*-Demethyl-4'-(*N*', *N*'-dimethyl-glycyl)-4 β -(4''-fluoroanilino)-4-desoxy-podophyllotoxin (9);

4'-*O*-Demethyl-4'-(*N*', *N*'-dimethyl-glycyl)-4 β -(4''-nitroanilino)-4-desoxy-podophyllotoxin hydrochloride (10);

4'-*O*-Demethyl-4'-(*N*', *N*'-dimethyl-glycyl)-4 β -(4''-fluoroanilino)-4-desoxy-podophyllotoxin hydrochloride (11);

5 4'-*O*-Demethyl-4'-glycyl-4 β -(4''-fluoroanilino)-4-desoxy-podophyllotoxin
(13); and

4'-*O*-Demethyl-4'-sarcosyl-4 β -(4''-fluoroanilino)-4-desoxy-podophyllotoxin
(14).

10 9. A compound according to claim 1, wherein said compound is
4'-*O*-Demethyl-4'-[(2'''-dimethylamino)-ethoxyl]-4 β -(4''-fluoroanilino)-4-
desoxy-podophyllotoxin.

10. A compound according to claim 1, wherein said compound is
15 4'-*O*-Demethyl-4'-[(2'''-dimethylamino)-ethylamino]-4 β -(4''-fluoroanilino)-4-
desoxy-podophyllotoxin.

11. A pharmaceutical formulation comprising a compound according to claim
1 in a pharmaceutically acceptable carrier.

20

12. The pharmaceutical formulation according to claim 11, wherein said
carrier is an aqueous carrier.

13. A method of treating a cancer, comprising administering to a subject in
25 need thereof a treatment effective amount of a compound according claim 1.

14. The method according to claim 13, wherein said cancer is selected from
the group consisting of skin cancer, lung cancer, Kaposi's sarcoma, testicular cancer,
lymphoma, leukemia, esophageal cancer, stomach cancer, colon cancer, breast cancer,

endometrial cancer, ovarian cancer, central nervous system cancer, liver cancer and prostate cancer.

- 5
15. The method according to claim 13, wherein said cancer is prostate cancer.
16. The method according to claim 13, wherein said cancer is colon cancer.
17. The method according to claim 13, wherein said cancer is lung cancer.
- 10
18. The method according to claim 13, wherein said cancer is breast cancer.
19. The method according to claim 13, wherein X is -NH-.
20. The method according to claim 13, wherein R¹ is phenyl.
- 15
21. The method according to claim 13, wherein R² is 2-dimethylamino-ethyl.